Correspondence

Angiomyofibroblastoma of the vagina

Angiomyofibroblastoma is a rare, recently described, soft tissue tumour that occurs mainly, but not exclusively, in the vulval region of premenopausal women.[1] We report a case arising in the vagina to draw the attention of pathologists to the fact that this rare neoplasm can occur outside the vulva.

A 54 year old woman, para 4 + 0, presented with a two year history of vaginal wall prolapse. Vaginal examination revealed a polypoid lesion on the anterior wall. Surgical removal and vaginal wall repair was performed.

The surgical specimen consisted of surface mucosa with an underlying well circumscribed, firm, homogenous, white coloured lesion measuring 2.5 cm in maximum diameter. Histology showed unremarkable surface squamous epithelium. Deep to this, a well circumscribed but unencapsulated lesion was present. This contained numerous randomly distributed blood vessels, most of which were thin walled and capillary-like (fig 1A), whereas others had thick muscular walls. The surrounding stroma contained spindle shaped cells, some with wavy nuclei (fig 1B), and others with a plasmacytoid or epithelioid appearance. Occasional multinucleate cells were present (fig 1B). There was little or no nuclear pleomorphism and mitotic figures were not identified. In some areas there was a tendency for concentration of the stromal cells around blood vessels, although this was not a prominent feature. The stroma contained collagen fibres and was focally oedematous with some extravasation of red blood cells. Immunohistochemical staining showed diffuse positivity of stromal cells for vimentin (Dako, Copenhagen, Denmark). There was focal strong staining for desmin (Dako) and occasional cells were weakly positive for α smooth muscle actin (Sigma, Poole, Dorset, UK). There was no staining of stromal cells for S100 protein (Diagnostic Products Ltd, Abingdon, UK), AE1/AE3 (Dako), CD34 (Serotec, Oxford, UK), or factor VIII related antigen (Signet, Ontario, Canada). Staining for α smooth muscle actin, CD34, and factor VIII highlighted the vascular channels. There was diffuse strong positivity of stromal cells for the oestrogen receptor (ER) (Dako) and progesterone receptor (PR) (Dako).

Within the vulva the chief differential diagnosis of angiomyofibroblastoma is likely to be aggressive angiomyxoma. Angiomyofibroblastoma is distinguished from aggressive angiomyxoma by its circumscribed border and higher cellularity, by the frequent presence of plump stromal cells, and by a lesser degree of stromal myxoid change. Angiomyofibroblastoma of the vulva is almost always a benign lesion which, unlike aggressive angiomyxoma, shows little or no tendency for local recurrence. However, a single case with sarcomatous transformation has been described.[2]

Since the original description, angiomyofibroblastoma has been described outside the vulva, in the female urethra and in the male genital tract, and there have been occasional reports of this neoplasm arising in the vagina.[3] In a report of 12 angiomyofibroblastomas, three had a vaginal location.[3] When situated within the vagina, the main differential diagnoses are likely to be a leiomyoma with prominent vascularity or an angiomyoma. However, diffuse immunoreactivity with antidesmin antibodies would be expected in both these lesions, rather than the focal positivity seen in our present case.

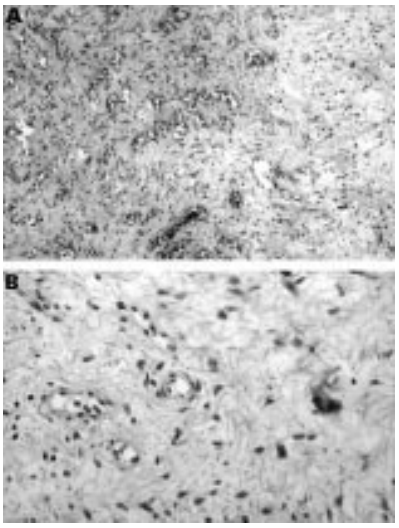

Figure 1 (A) Numerous capillary-like vascular channels are present within the neoplasm. (B) The stroma contains spindle shaped cells with occasional multinucleate cells.

The immunophenotype of angiomyofibroblastoma is not distinct but most cases are desmin positive and α smooth muscle actin negative. However, some are negative for desmin or positive for α smooth muscle actin. In this case, there was focal strong immunoreactivity for desmin, with only occasional cells staining with anti-α smooth muscle actin. Diffuse positivity for ER and PR was present and this has been described previously in vulval angiomyofibroblastoma.[4] Although this raises the possibility that angiomyofibroblastoma is a hormone responsive neoplasm, positivity for ER and PR might simply be a reflection of the presence of these receptors normally in the subepithelial stromal cells of the vulva and vagina. It is probable that angiomyofibroblastoma in this region is derived from mesenchymal cells in the subepithelial myxoid stromal zone, which extends from the endocervix to the vulva.[3] However, in a recent report this lesion has also been described in the fallopian tube.[5]

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1 Fletcher CDM, Tsang WYW, Fisher C, *et al*. Angiomyofibroblastoma of the vulva. A benign neoplasm distinct from aggressive angiomyxoma. *Am J Surg Pathol* 1992:**16**:373–82.
2 Nielsen GP, Young RH, Dickersin GR, *et al*. Angiomyofibroblastoma of the vulva with sarcomatous transformation ("angiomyofibrosarcoma"). *Am J Surg Pathol* 1997:**21**:1104–8.
3 Nielsen GP, Rosenberg AE, Young RH, *et al*. Angiomyofibroblastoma of the vulva and vagina. *Mod Pathol* 1996:**9**:284–91.
4 Laskin WB, Fetsch JF, Tavassoli FA. Angiomyofibroblastoma of the female genital tract. Analysis of 17 cases including a lipomatous variant. *Hum Pathol* 1997:**28**:1046–55.
5 Kobayashi T, Suzuki K, Arai T, *et al*. Angiomyofibroblastoma arising from the fallopian tube. *Obstet Gynecol* 1999:**94**:833–4.

Thrombophilia testing

In his recent leader, Dr Baglin gives an interesting overview of thrombophilia testing. However, his clinical practice of screening all unselected patients with an episode of venous thromboembolism is at odds with the British committee for standards in haematology guidelines on the investigation of thrombophilia.[2] According to these guidelines, the main indications for thrombophilia testing are patients with a venous thromboembolism before the age of 45 years, recurrent venous thrombosis or thrombophlebitis, thrombosis in an unusual site, or a first venous thromboembolism with a clear family history of venous thrombosis. Such restrictions on expensive and time consuming thrombophilia tests to patient groups more likely to have underlying thrombophiliac defects are almost mandatory for haematology departments working under the financial constraints of the present day national health service.

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1 Baglin T. Thrombophilia testing: what do we think the tests mean and what should we do with the results? *J Clin Pathol* 2000;**53**:167–70.
2 The British Committee for Standards in Haematology. Guidelines on the investigation and management of thrombophilia. *J Clin Pathol* 1990;**43**:703–9.

A comparison of international normalised ratio (INR) measurement in hospital and general practice settings: evidence for lack of standardisation

Previous reports of discrepancies in international normalised ratio (INR) measurement between centres have focused on hospital based methodologies.[1–3] Previously, we have demonstrated differences in derived INR values for the same sample tested in primary care and in one of three different haematology laboratories.[4] Our present study is an extension of the previous one, investigating comparative results based on contemporaneous samples measured in one primary care centre and in two hospital laboratories using a variety of techniques.

Venous blood was drawn from patients in one primary care centre over a three month period. The sample was tested on site for INR estimation using the Thrombotrak NPT and Thrombotest reagent. The remainder of the venous sample was placed in a citrated collection bottle and sent to two reference laboratories routinely used by the general practitioner to measure INR values (laboratories 1 and 2). Laboratory 1 determined INR values using three separate methods: a Thrombotrak using Thrombotest, an ACL machine using IL reagent, and a KC-10 machine using Manchester reagent. Laboratory 2 determined INR values using a KC-10 machine with Manchester reagent. Because laboratory 1 acts as the regional reference laboratory and uses the ACL/IL combination as its routine

Table 1 Mean difference (SEM) in INR between methods (n = 54)

	ACL Lab 1	*KC-10 Lab 1*	*KC10 Lab 2*	*Thrombotrak*
Thrombotrak: Lab 1	0.25 (0.04)**	0.50 (0.05)**	0.35 (0.06)**	−0.06 (0.04)
ACL: Lab 1		0.24 (0.03)**	0.11 (0.05)*	−0.31 (0.05)**
KC-10: Lab 1			−0.13 (0.06)*	−0.55 (0.07)**
KC-10: Lab 2				−0.42 (0.07)**

*, $p < 0.05$; **, $p < 0.001$.
INR, international normalised ratio.

method of INR testing, the result obtained was taken as the gold standard. Samples were sent to the laboratory using routine transport with no samples tested more than 12 hours after venesection.

Fifty four separate venous samples from 26 patients were sent from the practice to the laboratories. The INR values obtained ranged from 1.0 to 6.1. Table 1 shows the mean difference in results from the various machines. There was a significant mean difference in the practice Thrombotrak results relative to the ACL and the KC-10 in both laboratories, but none between practice measurements and those obtained in laboratory 1 using the same technology. There were also significant differences between all hospital systems. Furthermore, there was a significant difference between ACL and KC-10 results from the same laboratory and between KC10 results from different laboratories.

Our results suggest that regular differences occur in INR measurements obtained on the same samples using different methodologies and draws attention to inherent problems associated with INR measurement in different settings. The clinical implication of these findings is that patients could receive different doses of warfarin depending upon which centre monitors their INR. Nevertheless, the best agreement to be found was between the practice derived INR and the laboratory derived INR using the same technology. This shows that primary care INR estimations are as reliable as laboratory estimations using the same combination of reagents and technology. Therefore, it follows that as long as continuity of INR estimation by location and method is maintained for individual patients, the rate of unnecessary warfarin dose adjustments will be reduced.

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1 Eckman MH, Levine HJ, Pauker SG. Effect of laboratory variation in the prothrombin-time ratio on the results of oral anti-coagulant therapy. *N Engl J Med* 1993;**329**: 696–701.
2 Morrison M, Fitzsimons EJ. Discrepant INR values strike again. *Clin Lab Haematol* 19991; **13**:221–5.
3 Morrison M, Fimls G, Caldwell A. Discrepant INR values: a comparison between Manchester and Thrombotest reagents using capillary and venous samples. *Clin Lab Haematol* 1989;**11**: 393–8.
4 Hobbs FDR, Fitzmaurice DA, Murray ET, *et al*. Is the international normalised ratio (INR) reliable? A trial of comparative measurements in hospital laboratory and primary care settings. *J Clin Pathol* 1999;**52**:494–7.

Book reviews

Diagnostic Surgical Pathology. Volumes 1 and 2, 3rd ed. Sternberg SS, ed. ($325.) Lippincott, 1999. ISBN 0 3975 8792 9.

At 56 chapters written by 93 authors and extending to 2445 pages, this is the third edition of Sternberg's *Diagnostic Surgical Pathology* and a heavy weight re-entry into the mighty two and three volume all embracing histopathology tome market. The preface by the editor and his four associates promises us "the latest on PMETs". I am not quite sure what PMETs are. Perhaps they are secondary deposits from PNETs! Typographical errors aside, on a more positive note, the promise of a revised lymphoma classification, an update on gut lymphomas and those of the skin, a reclassification of papillary urothelial neoplasms, the introduction of new aspects of kidney tumours, modernisation of the approach to gastrointestinal stromal tumours, new concepts in ductal carcinoma in situ of the breast and handling of breast specimens, and an update of chapters on urothelial and paediatric neoplasms is well met. There is substantial new information in this edition. The references appear to cut out in late 1998 which, given the complexity of editing a work of this magnitude, probably represents the most up to date information that can be expected. Although the sections on new diagnostic techniques such as molecular biology have been expanded, the work remains grounded in diagnostic histopathology. The general background to each disease process is well described and the clinicopathological correlations are dealt with well; this book is well placed to inform multidisciplinary care.

The transition to almost all full colour illustrations is heralded as a major advance to this edition. Although many of the pictures are of good quality and many do add information that could not be obtained from a monochrome image, the quality of the colour reproduction does vary enormously between the chapters. For example, that by R R Heffner on muscle biopsy in neuromuscular disease has excellent illustrations, whereas that by A M Hanby and two other authors on the breast has particularly poor ones, with some of the worst examples of colour casts and low contrast in any current professional textbook. I do not think that the editors should have let this through. The scope of the textbook is very wide and the depth of knowledge and discussion achieved is commendable, but again this is a point that varies from chapter to chapter, suggesting some editorial inconsistency.

More fundamental questions are: What is the purpose of giant multiauthor texts like this, who needs them, when will they be used and how, and if they are required, what is the "pecking order" for choice of these? Very often better written, more detailed, and more up to date descriptions exist in system specific texts. The constraints of producing a multi author work like this mean that the individual chapters are unlikely to rival the detail of the specialised book. However, I suspect most of us consult books like this on the areas in which we do not have specialised texts. Apart from this text, this market segment appears to include *Ackerman's Surgical Pathology* edited by Rosai, *Anderson's Pathology* edited by Damjanov and Linder, and Silverberg's *Principles and Practice of Surgical Pathology*. Perhaps the *Oxford Textbook of Pathology* is not a direct competitor because its remit is so different. The choice of which of these books to consult is a personal matter, depending on preferred style and balance of writing. In my view, Ackerman is particularly commendable for Rosai's masterful treatment of differential diagnosis in surgical pathology, Silverberg is brief and to the point, yet quite detailed, and *Anderson's Pathology* is good for clinicopathological correlations and the general context of disease. This text lies somewhere in the middle, meeting several of the purposes, but to my mind it is beaten for quality of histological description by the first two works, although still very worthwhile if funds allow its purchase.

T J STEPHENSON

Atlas of Immunology. Cruse JM, Lewis RE. (£49.50.) Springer-Verlag, 1999. ISBN 3 540 64807 0.

The *Atlas of Immunology* aims to be "the most up to date and thoroughly illustrated treatise available". Sadly the book does not achieve what it sets out to do. Many of the images by their nature attempt to illustrate clinical or clinical laboratory situations and, particularly for these, the highest quality of image is required to enable the differentiation from other often subtly different conditions. Many clinical images are given simply as line drawings—for example, a malar rash in systemic lupus erythematosis, the hands in systemic sclerosis, or a baby with an intravenous line (the image for severe combined immunodeficiency). A dermatology text would not accept line drawings of a malar rash and why should immunologists? It is as if a team of journalists have collected as many images as possible regardless of quality, content, or currency. All are printed in black and white, and the reproduction is often poor. No explanation is given to any figure, either in the text, or in the legends, which are all simple statements such as "release of sequestered antigen". For images such as indirect immunofluorescence of salivary gland duct showing the staining pattern of anti-salivary gland antibodies labelled simply as "Sjögren's syndrome" this is especially uninformative. Even the accompanying text is now largely outdated.

This ambitious project was an opportunity for two distinguished authors to provide the reader with access to a lifetime's collection of first class images, using each one as an explanation of a key immunological concept. Each would have a detailed explanation, describing the distinguishing features, and contrasting it with similar images. As a minimum it would

use colour, and preferrably would be on CD-ROM and have internet links to images so that they could be incorporated into teaching material. This opportunity has been missed.

W A C SEWELL

Microbiology in Clinical Practice, 3rd ed. Shanson DC. (£29.99.) Butterworth Heinemann, 1999. ISBN 0 7506 3110 4.

With the dramatic fall in professors of medical microbiology, together with the recommended reduction in didactic teaching of medical students, the requirement for a readable and affordable textbook assumes even more importance. Although the would be doctors of tomorrow do not necessarily see it like that—plenty of money for the pleasures of life, but none for books. David Shanson's *Microbiology in Clinical Practice* has been a recommended text for medical students throughout the UK since its launch in 1982. So what has changed since the first edition? New diseases and new pathogens have emerged such as *Helicobacter pylori*; hepatitis C, E, and G; *Escherichia coli* 0157; *Bartonella*; *Chlamydia pneumoniae*; and variant CJD—to name but a few. In addition to the new, we welcome back the old: diphtheria and tuberculosis. The ever ingenious bacteria appear to have the upper hand against the pharmaceutical chemist, and the global epidemic of AIDS marches ever onwards, ever confident into this new millennium. In an attempt to aid the would be Alexander Flemings of the future to climb out of their Petri dishes and discard the loop, an additional chapter entitled "Applications of molecular biology to clinical microbiology and infectious diseases" has been added. This highly readable textbook is recommended to medical students, MLSOs, infection control nurses, and general practitioners alike. Value for money at £29.99—all for the price of a few beers!

R C SPENCER

Laboratory-acquired Infections: History, Incidence, Causes and Preventions, 4th ed. Collins CD, Kennedy DA. (£45.00.) Butterworth Heinemann, 1999. ISBN 0 7506 4023 5.

This is the fourth edition of this excellent book, which is found on the shelves of most microbiology laboratories in the UK. In the 16 years since the first edition it has grown from 13 to 19 chapters to take account of recent developments in infections and agents such as new variant CJD, risk assessment, and European regulations and recommendations.

The book is full of practical advice on avoiding laboratory hazards, such as aerosol generation and sharps injury, as relevant now as in the days before disposable equipment and test formats. It also provides a fascinating list of published reports of laboratory acquired infections and is the standard UK reference source for these.

The strength of this book lies in its detailed coverage of all aspects of laboratory practice and management, which is backed up by reference to appropriate health and safety regulations or guidelines. For example, there is an excellent comprehensive chapter on safety cabinets and a helpful section on transport of isolates and samples, although the latter does not discuss the recent UK post office changes.

Some of the references are a little out of date, such as 1982 for a text on bacterial pathogenesis, and there are occasional errors, but the overall quality of the book is as high as ever.

Everyone working in a laboratory setting should have to read this book, especially those with little experience of working with viable organisms or clinical samples, such as those taking up genetic manipulation work. It remains thoroughly recommended.

C KIBBLER

Proton Pump Inhibitors. Olbe L, ed. (£92.00.) Birkhauser, 1999. ISBN 3 7643 5897 1.

In the past decade, proton pump inhibitors have dramatically changed the treatment of acid related disorders. They profoundly suppress gastric acid, without the development of tolerance or side effects, and are very commonly used. As such, this book edited by Dr Olbe is of interest to clinicians, physiologists, and pharmacists. The book is written by experts in the field and largely consists of two sections on pharmacology and clinical effects. The first section covers among others the mechanism of action and the consequences of acid inhibition in animals and humans. The second section focuses on the use of proton pump inhibitors for ulcer disease, Zollinger-Ellison syndrome, and gastro-oesophageal reflux disease. Thus, the book deals with many topics. Unfortunately, the subject index is limited, which hampers its use as a quick reference. Furthermore, several currently relevant issues are not, or only briefly, discussed. These include the new formulation of omeprazole in a multiple pellet solution, the use of intravenous formulations for upper gastrointestinal bleeding, the possibility of nocturnal acid breakthrough and fundic gland polyp formation during treatment, as well as that of rebound hypersecretion after the withdrawal of treatment. Finally, the topic of *Helicobacter pylori* and atrophic gastritis is discussed repeatedly, but only some of the arguments mentioned in the international literature are brought forward. Therefore, a second edition of the book would benefit from such updating for clinicians who are interested in the newest aspects of proton pump inhibitor treatment.

E J KUIPERS

Calendar of events

Full details of events to be included should be sent to Maggie Butler, Technical Editor JCP, The Cedars, 36 Queen Street, Castle Hedingham, Essex CO9 3HA, UK; email: maggiebutler@pilotree.prestel.co.uk

Applications and Techniques in Veterinary Pathology
5 October 2000, Royal College of Pathologists, London, UK
Further details: Maureen Russell, Scientific Meetings Officer, Royal College of Pathologists, 2 Carlton House Terrace, London SW1Y 5AF, UK. (Tel +44 (0)20 7451 6740; email www.rcpath.org)

New Millenium Bugs
18 October 2000, Royal College of Pathologists, London, UK
Further details: Maureen Russell, Scientific Meetings Officer, Royal College of Pathologists, 2 Carlton House Terrace, London SW1Y 5AF, UK. (Tel +44 (0)20 7451 6740; email www.rcpath.org)

Practical Adult Cardiovascular Pathology Course
6–8 November 2000, Royal Brompton Hospital, Imperial School of Medicine, National Heart and Lung Institute
Further details: Short Course Office, National Heart and Lung Institute, Dovehouse Street, London SW3 6LY, UK. (Tel +44 (0)20 73518172; fax +44 (0)20 7351 8246; email shortcourse.NHLI@IC.AC.UK)

Practice Guidelines for Non-Hodgkin's Lymphoma
21–22 November 2000, Royal College of Pathologists, London, UK
Further details: Maureen Russell, Scientific Meetings Officer, Royal College of Pathologists, 2 Carlton House Terrace, London SW1Y 5AF, UK. (Tel +44 (0)20 7451 6740; email www.rcpath.org)

Cytopathology Update: Making Cervical Cytopathology Work
7 December 2000, Royal College of Pathologists, London, UK
Further details: Maureen Russell, Scientific Meetings Officer, Royal College of Pathologists, 2 Carlton House Terrace, London SW1Y 5AF, UK. (Tel +44 (0)20 7451 6740; email www.rcpath.org)

Diagnostic Gynaecological Pathology
13–15 January 2001, The Embassy Suites, Palm Desert, California, USA
Further details: Department of Continuing Education, Harvard Medical School, 25 Shattuck Street, Boston, MA 02115, USA. (Tel +1 617 432 1525; fax +1 617 432 1562; email hms-cme@hms.harvard.edu)

Urological Surgical Pathology for the Practising Pathologist
24–26 March 2001, Sanibel Harbour Resort and Spa, Fort Myers, Florida, USA
Further details: Department of Continuing Education, Harvard Medical School, 25 Shattuck Street, Boston, MA 02115, USA. (Tel +1 617 432 1525; fax +1 617 432 1562; email hms-cme@hms.harvard.edu)

6th European Forum on Quality Improvement in Health Care
29–31 March 2001, Bologna, Italy
Further details: BMA/BMJ Conference Unit, BMA House, Tavistock Square, London WC1H 9JR, UK. (Tel +44 (0)20 7383 6409; fax +44 (0)20 7383 6869; email Quality@bma.org.uk; website www.quality.bmjpg.com)